REMARKS

The specification has been amended to correct typographical errors concerning cited patents and extra words and letters. It is submitted that no new matter has been introduced by the foregoing amendments. Approval and entry of the amendments is respectfully solicited.

Anticipation Rejection

Claim 28 was rejected under 35 USC §102(b) as anticipated by Sunshine *et al.*, US Patent No. 4,783,465 ("Sunshine 1"). (Paper No. 10202004 "Office Action" at 2.)

For the reasons set forth below, the rejection, respectfully is traversed.

Sunshine 1 discloses

[57] **ABSTRACT**

Pharmaceutical compositions and methods of using same comprising a non-steroidal anti-inflammatory drug in combination with a non-sedating antihistamine and optionally one or more other active components selected from a decongestant, cough suppressant (antitussive) or expectorant are provided for the relief of cough, cold, cold-like and/or flu symptoms and the discomfort, pain, headache, fever and general malaise associated therewith.

In the pharmaceutical compositions and methods of the present invention, the foregoing active ingredients will typically be administered in admixture with suitable pharmaceutical diluents, excipients or carriers (collectively referred to herein as "carrier" materials) suitably selected with respect to the intended form of administration, i.e., oral tablets, capsules, elixirs, syrups, suspensions, etc. and consistent with conventional pharmaceutical practices. For instance, for oral administration in (Col. 12)

4,783,

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natural sugars, corn sweeteners, natural and synthetic gums such as acacia, sodium alginate, carboxymethylcellulose, polyethylene glycol and waxes. Among the lubricants there may be mentioned for use in these dosage forms, boric acid, sodium benzoate, sodium acetate, sodium chloride, etc. Disintegrators include, without limitation, starch, methylcellulose, agar, bentonite, guar gum, etc. Sweetening and flavoring agents and preservatives can also be included where appropriate.

In making the rejection, the Examiner contended that "Sunshine teach a pharmaceutical composition comprising an NSAID combined with a non-sedating antihistamine and optionally one or more decongestants (amines) (Office Action at 2.) The Examiner further contended that the compositions are "administered in admixtures in the form of *inter alia* suspensions."

As is well settled, anticipation requires "identity of invention." Each and every element recited in a claim must be found in a single prior art reference and arranged as in the claim. Furthermore, in a §102(b) rejection there must be no difference between what is claimed and what is disclosed in the applied reference. The Examiner is required to point to the disclosure in the reference "***by page and line***" upon which the claim allegedly reads.

The rejection fails to identify where in Sunshine 1 each and every element of claim 28 is shown. In particular, the rejection does not recite where there is a disclosure of the claimed stable suspension. That was the Examiner's burden. Because the Examiner did not meet the minimum requirements for the instant rejection, it is improper and should be withdrawn.

Obviousness Rejections

Claims 28-41 were rejected under 35 USC §103(a) as being unpatentable over U.S. Pat. No. 4,552,899 ("Sunshine 2") (Office Action at 4.)

For the reasons set forth below the rejection, respectfully is traversed.

Sunshine discloses

Pharmaceutical compositions and methods of using same comprising a non-steroidal anti-inflammatory drug in combination with at least one other active component selected from an antihistamine, decongestant, cough suppressant (antitussive) or expectorant are provided for the relief of cough, cold and cold-like symptoms. Abstract;.

It is, therefore, a primary object of the present invention to provide pharmaceutical compositions of matter comprising an analgesically effective amount of a non-steroidal anti-inflammatory drug (NSAID) in combination with at least one of an antihistamine, decongestant, cough suppressant, expectorant and, optionally, including pharmaceutically acceptable carriers therefor. Col. 1.

The non-steroidal anti-inflammatory drugs (NSAID's) for use in the pharmaceutical compositions and methods of use of the present invention may be selected from any of the following categories:

(1) The propionic acid derivatives;
(2) The acetic acid derivatives;
(3) The fenamic acid derivatives;
(4) The biphenylcarboxylic acid derivatives; and
(5) The oxicams.

Accordingly, the term "NSAID" as used herein is intended to mean any non-narcotic analgesic non-steroidal anti-inflammatory compound, including the pharmaceutically acceptable non-toxic salts thereof, falling within one of the five structural categories above but excluding aspirin, acetaminophen and phenacetin. Col. 3.

Of the propionic acid derivatives for use herein, ibuprofen, naproxen, flurbiprofen, fenoprofen, ketoprofen, suprofen, fenbufen, and fluprofen may be mentioned as particularly preferred compounds.

Of the acetic acid derivatives, presently preferred members include tolmetin sodium, zomepirac, sulindac and indomethacin.

Of the fenamic acid derivatives, particularly preferred compounds include mefenamic acid and meclofenamate sodium.

The particularly preferred biphenylcarboxylic acid derivatives for use in the present invention include diflunisal and flufenisal.

The particularly advantageous oxicams include piroxicam, sudoxicam and isoxicam. Col. 3.

preferred.

With respect to the dosage amount of the non-steroidal anti-inflammatory drugs in the compositions of the invention, although the specific dose will vary depending upon the age and weight of the patient, the severity of the symptons, the incidence of side effects and the like, for humans, typical effective analgesic amounts of presently preferred NSAID's for use in unit dose compositions of the invention are about 100–500 mg diflunisal, about 25–100 mg zomepirac sodium, about 50–400 mg ibuprofen, most preferably 100–200 mg, about 125–500 mg naproxen, about 25–100 mg flurbiprofen, about 50–100 mg fenoprofen, about 10–20 mg piroxicam, about 125–250 mg mefenamic acid, about 100–400 mg fenbufen or about 25–50 mg ketoprofen; however, greater or lesser amounts may be employed if desired or necessary. With respect to the compounds set forth hereinabove falling within the propionic acid derivative category, suitable dosage ranges for these compounds will generally fall within the range of 25 mg to 600 mg in each unit dose.

A complete description of the various NSAID's, including acceptable analgesically effective amounts thereof for use in unit dose compositions of the present invention also appears in applicants co-pending U.S. application Ser. Nos. 474,358, filed Mar. 11, 1983 and 578,288, filed Feb. 8, 1984, the entire disclosures of which are incorporated herein by reference.

Col. 4.

In the pharmaceutical compositions and methods of the present invention, the foregoing active ingredients will be combined with the non-steroidal anti-inflammatory drug(s) and will typically be administered in admixture with suitable pharmaceutical diluents, excipients or carriers (collectively referred to herein as "carrier" materials) suitably selected with respect to the intended form of administration, i.e., oral tablets, capsules, elixirs, syrups, etc. and consistent with conventional pharmaceutical practices. For instance, for oral administration in the form of tablets or capsules, the active drug components may be combined with any oral non-toxic pharmaceutically acceptable inert carrier such as lactose, starch, sucrose, cellulose, magnesium stearate, dicalcium phosphate, calcium sulfate, mannitol, ethyl alcohol (liquid forms) and the like. Moreover, when desired or necessary, suitable binders, lubricants, disintegrating agents and coloring agents can also be incorporated in the mixture. Suitable binders include

Col. 5.

starch, gelatin, natural sugars, corn sweeteners, natura
and synthetic gums such as acacia, sodium alginate
carboxymethylcellulose, polyethylene glycol anc
55 waxes. Among the lubricants there may be mentionec
for use in these dosage forms, boric acid, sodium benzo
ate, sodium acetate, sodium chloride, etc. Disintegra
tors include, without limitation, starch, methylcellulose
agar, bentonite, guar gum, etc. Sweetening and flavor
60 ing agents and preservatives can also be included where
appropriate.

Col. 6.

In making the rejection, the Examiner asserted that Sunshine "combines NSAID's such as ibuprofen in doses of from 50 to 400 mg or in general, propionic acid derivatives in doses of from 25 mg to about 600 mg with pseudoephedrine for use as a preserved syrup formulation (column 12-13, lines 50-9)." (Office Action at 4.). The Examiner further asserted that "[t]he composition is administered in admixture with suitable pharmaceutical diluents, excipient and carriers suitably selected with respect to the intended form of administration, i.e., oral tablets, capsules, elixirs, syrups, etc." (*Id.*)

The Examiner acknowledged, however, that Sunshine 2 differs from the presently claimed invention in that "[i]t does not specifically recite a suspension." (Office Action at 4.)

To fill the acknowledged gap, the Examiner relied upon the fact that ibuprofen is not soluble in water and "as such would necessarily be suspended in [] syrup" (*Id.*)

The Examiner then concluded that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a suspension base." (*Id.*)

As is fundamental, a *prima facie* case of obviousness must be based on facts, "cold hard facts." *In re Freed*, 165 USPQ 570, 571-72 (C.C.P.A. 1970). When the rejection is not supported by facts, it cannot stand. *Ex parte Saceman*, 27 USPQ2d 1472, 1474 (B.P.A.I. 1993).

"Determination of obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention." ATD Corp. v. Lydall, Inc., 159 F.3d 534, 546, 48 USPQ2d 1321, 1329 (Fed.

Cir. 1998). There must be a teaching or suggestion within the prior art, within the nature of the problem to be solved, or within the general knowledge of a person of ordinary skill in the field of the invention, to look to particular sources, to select particular elements, and to combine them as combined by the inventor. See Ruiz v. A.B. Chance Co., 234 F.3d 654, 665, 57 USPQ2d 1161, 1167 (Fed. Cir. 2000); ATD Corp, 159 F.3d at 546, 48 USPQ2d at 1329; Heidelberger Druckmaschinen AG v. Hantscho Commercial Prods., Inc., 21 F.3d 1068, 1072, 30 USPQ2d 1377, 1379 (Fed. Cir. 1994) ("When the patented invention is made by combining known components to achieve a new system, the prior art must provide a suggestion or motivation to make such a combination.").

For a *prima facie* case of obviousness to be established, the teachings from the prior art itself must appear to have suggested the claimed subject matter to one of ordinary skill in the art. *See In re Rinehart*, 189 USPQ 143, 147 (CCPA 1976). The mere fact that the prior art could be modified as proposed by the Examiner is not sufficient to establish a *prima facie* case of obviousness. *See In re Fritch*, 23 USPQ 1780, 1783 (Fed. Cir. 1992).

It is respectfully submitted that it is not seen where the record contains any facts to support the Examiner's conclusory statement that having ibuprofen, which is water insoluble, in a syrup would necessarily lead to the ibuprofen being suspended in the syrup.

The Examiner's conclusion appears to be premised on the fact that the syrup must have water. There are no facts in the record made by Examiner nor can it located where the syrup disclosed by Sunshine 2 would have any water in it.

Even if it did disclose water, which is not agreed with for the above reasons, merely disclosing a water insoluble compound in water does not make a suspension. It is respectfully submitted that such a disclosure would disclose a syrup that would require the composition to be shaken to disperse the water insoluble compound in the syrup as

the water insoluble compound would fall out of the syrup over time. Such a syrup would not be a suspension.

For these reasons, the rejection is improper and should be withdrawn.

Obviousness-type Double Patenting

Claims 18-27 were ejected under the judicially created doctrine of obviousness-type double patenting. (Office Action at 6.) The Examiner alleges that claims 18-27 of the instant application "are unpatentable over claims 1-13 of U.S. Patent No. 6,211,246.

In making the rejection, the Examiner alleged that "[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the patent are drawn to a method for enhancing the absorption rate of an amine comprising administering a stable liquid form of the composition comprising an amine and a NSAID. The claims of the instant application are drawn to a suspension." (*Id.*)

Upon notification by the Examiner that claims 18-27 are allowable but for this rejection, the option of filing a Terminal Disclaimer will be addressed.

Claims 29-41 also have been rejected under the judicially created doctrine of obviousness-type double patenting. (Office Action at 6.) The Examiner alleges that claims 29-41 of the instant application "are unpatentable over claims 23-30 of U.S. Patent No. 6,211,246.

In making the rejection, the Examiner alleged that "the claims are drawn to a liquid suspension. The claims of the patent are drawn to a stable liquid composition with dependent claims to a suspension." (*Id.*)

Upon notification by the Examiner that claims 29-41 are allowable but for this rejection, the option of filing a Terminal Disclaimer will be addressed.

Claim 42 was rejected under the judicially created doctrine of obviousness-type double patenting. (Office Action at 7.) The Examiner alleges that claim 42 of the instant application "are unpatentable over claim 14 of U.S. Patent No. 6,211,246.

In making the rejection, the Examiner alleged that "the claim is drawn to a suspension of claim 30 wherein the suspension further comprises xanthan gum, pregelatinized starch, polyoxyethylene sorbitan monooleate and a taste masking agent selected from sugar, sweet polydhydric alcohol, cyclamates, aspartame, sucralose, saccharin, flavoring agents and mixtures thereof." The Examiner also alleged that "claim 14 of the patent is drawn to composition comprising a pharmacologically effective amount of amine and a pharmacologically amount of a NSAID wherein the amine and the NSAID are in a stable liquid suspension and further comprise all the elements of instant claim 42. The claims are the same when the limitations of claims 20 and 28 are taken into consideration, from which instant claim 42 depends."

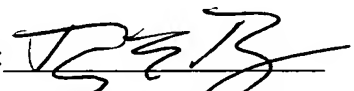
The Examiner further indicated that claim 42 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and with a timely filed terminal disclaimer.

Upon notification by the Examiner that claims 18-41 are allowable but for this rejection, the option of filing a Terminal Disclaimer will be addressed.

Accordingly, for the reasons set forth above, entry of the amendments, withdrawal of the rejections and objections, and allowance of the claims is respectfully requested.

Finally, the Examiner is invited to call the applicants' undersigned representative if any further action will expedite the prosecution of the application or if the Examiner has any suggestions or questions concerning the application or the present Response. In fact, if the claims of the application are not believed to be in full condition for allowance, for any reason, the applicants respectfully request the constructive assistance and suggestions of the Examiner in drafting one or more acceptable claims pursuant to MPEP § 707.07(j) or in making constructive suggestions pursuant to MPEP § 706.03 so that the application can be placed in allowable condition as soon as possible and without the need for further proceedings.

Respectfully submitted,

By: 

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